

FIG.1

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graph TD
    A[Prepar Master Cell Stock MCS] --> B[Prepare MCS+n]
    A --> C[Genetically Alter PRRS Virus]
    B --> D[Prepare Working Cell Stock]
    B --> E[Plaque-purify Genetically Altered Vaccine Virus 3 Times]
    D --> F[Prepare Prototype Vaccine MSV(X+5)]
    D --> G[Prepare Working Seed Virus MSV(X+4)]
    E --> H[Prepare Master Seed Virus MSV(X), MSV(X+1), MSV(X+2) and MSV(X+3)]
    H --> G
    G --> I[Develop Pig Challenge Models]
    G --> J[Develop Clinical Assays]
    I --> K[Perform Efficacy Studies]
    J --> K
    L[Develop Potency Assay] --> K
    K --> M[Perform Safety Studies]
    M --> N[Submit Research Data to NVSL]
    N --> O[Obtain Vaccine License]
  
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FIGURE 2

ISU-12 cDNA λ Library Construction

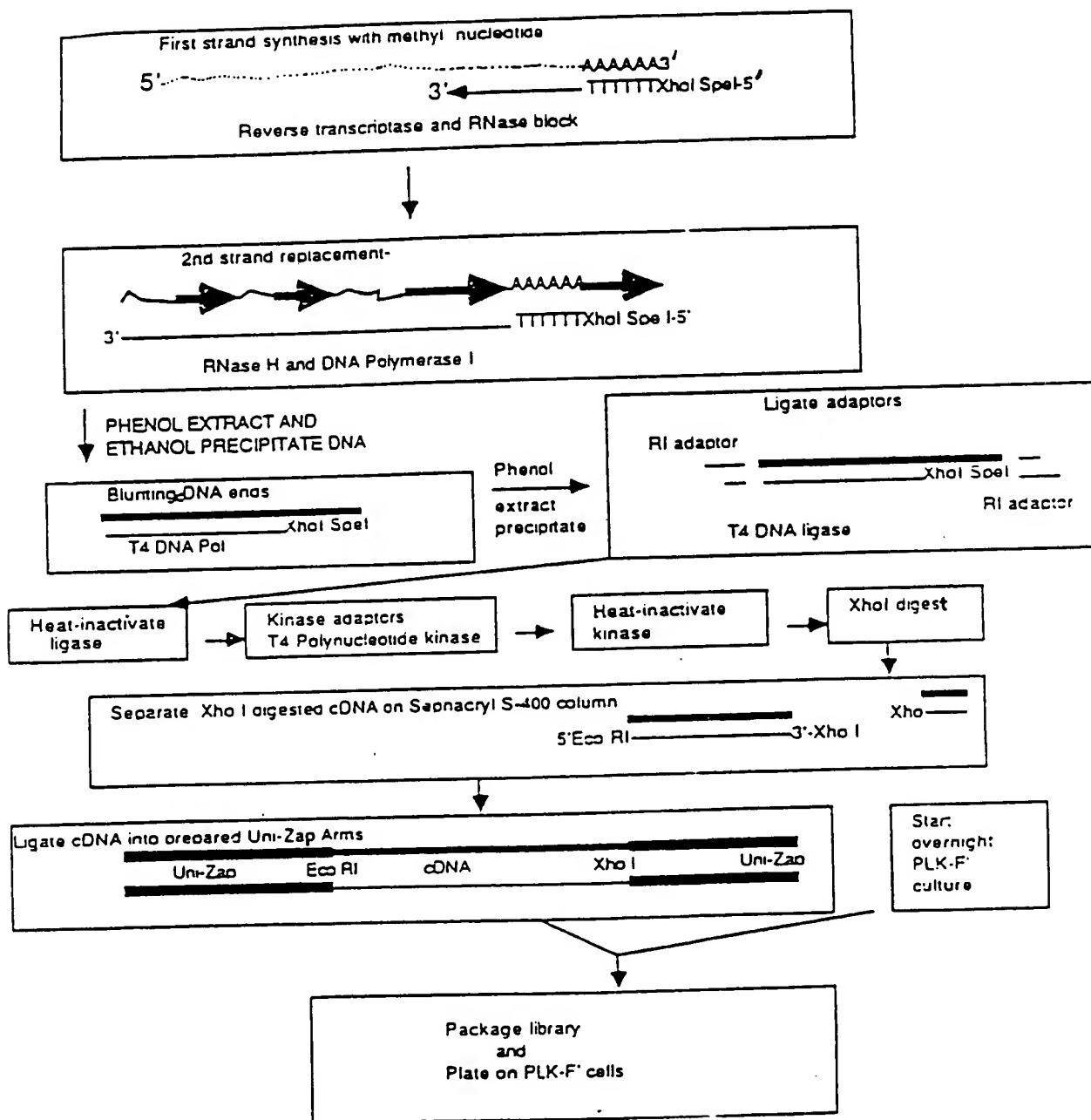


FIGURE 3

Identification of ISU-12 Authentic Clones by Differential Hybridization

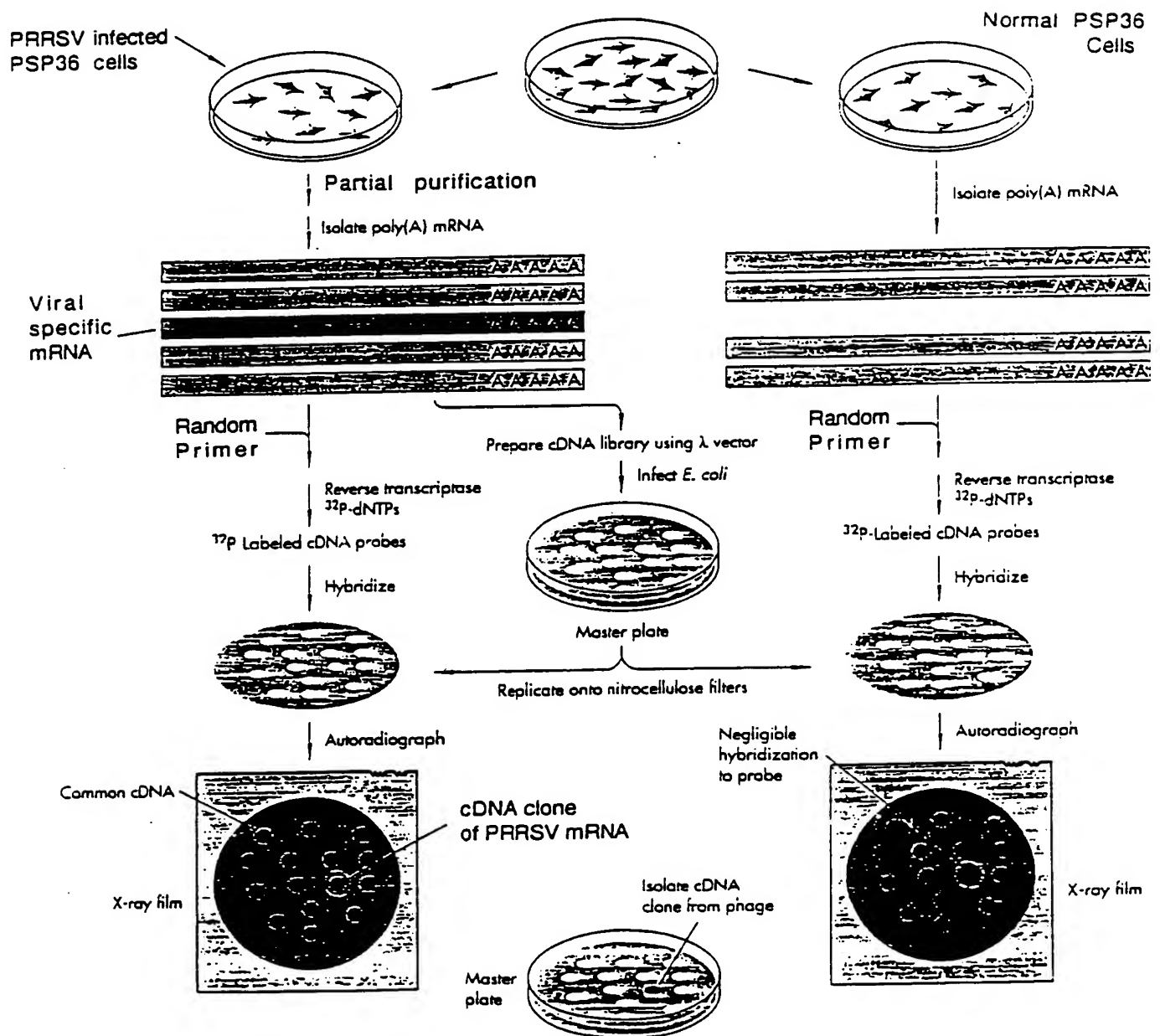


FIGURE 4

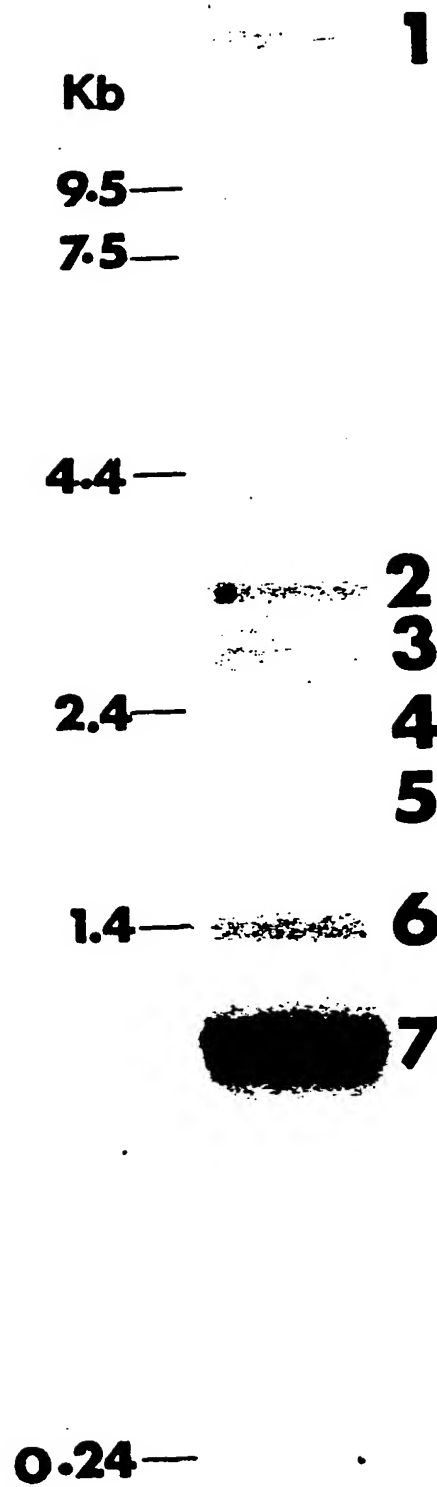


FIGURE 5

ISU-12-7a 3' terminal Graphics

FIGURE 6

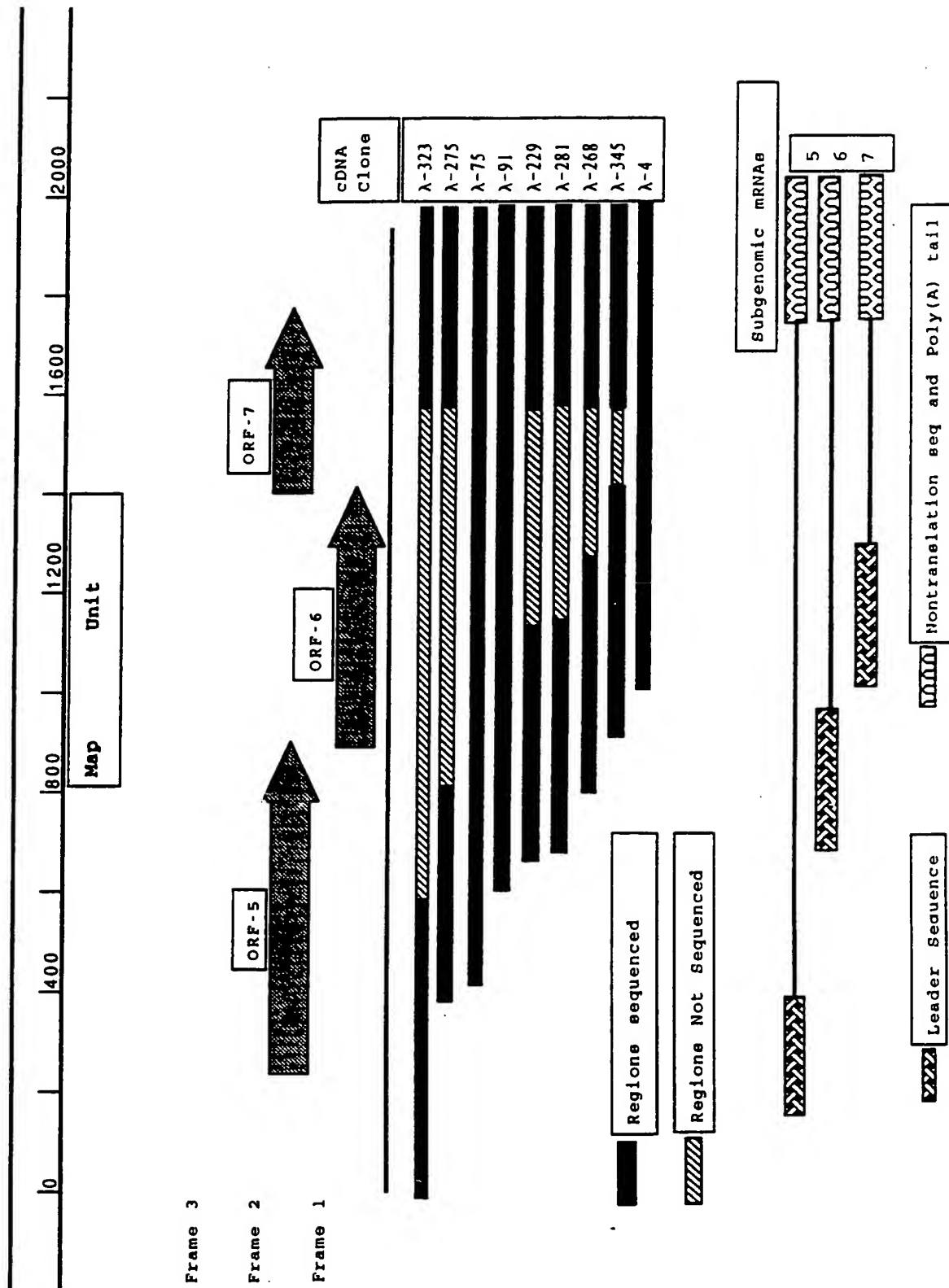


FIGURE 7

GGCAGGCTTTGCTGTCTCCCAAGACATCAGTTGCCCTTAGGCATCGCAACTCGGCCTCTGAGGCGATTTCGCAAAGTCCCTCAGTGC CGCACGGCGATAGGG 100

ACACCCGCTGTATATCACTGTTCACAGCCAATGTTACCGATGAGAAATTATTTGCATTCTCTGATCTTCTCATGCTTTCTTCTGCTTTTCTATGCTTCTG 200

AGATGAGTGAAAAGGGATTTAAGGTGGTATTTTGGCAATGTGTACGGCATCGTGGCAGTGTGCGTCAACTTCACCAGTTACGTCCAACATGTCAAGGAATT 300

TACCCAAAGCTTCTTGGTAGTTGACCATGTGCGGCTGCTCCATTTTCATGACGCCCCGAGACCATGAGGTGGGCAACTGCTTTTAGCTGTCTTTTGGCATT 400

CTGTGTGCAATTTGAATGTTTAAGTATGTTGGGAAATGCTTGACCGCGGCTGTGTCTCGCAATTGCTTTTGTGGTGTATCGTGCCGCTCTGTGTTT 500

*** ORF4 stop +1>ORF5 start

GTTGCGCTCGTACGCGCAACGGGAACAGCGGCTCAAATTTACAGCTGATTTTACAACCTTGACGCTATGTGAGCTGAATGGCACAGATTGGCTAGCTAATA 600

AATTTGACTGGGCAGTGGAGTGTTTTGTCATTTTCTCTGTGTGACTCACATGTCTCTTATGGTGGCCCTCACTACTAGCCATTTCTTTGACACAGTCCG 700

TCTGGTCACTGTGTCTACCGCTGGGTTTGTTCACGGGCGGTATGTTC TGAGTAGCATGTACGCGGCTGTGCGCTGGCTGGCTTGATTTGCTTTCGTCATT 800

AAGCTTTCGAAGAATTGCATGTCTGGCGCTACTCATGTACAGATAATACCAACTTTCTTCTGGACACTAAGGGCAGACTCTATCGTTGGCGGTCGCGCTG 900

TCATCATAGAGAAAAAGGGCAAAGTTGAGGTGGAAGGTACCTGATCGACCTCAAAAGAGTTGTGCTTGATGGTTTCGCGGCTACCCCTGTAAACAGAGT 1000

***ORF6 start +1> ***ORF5 stop

TTTAGCGGAACAATGAGAGTGTCTCTAGATGACTTCTGTTCATGATAGCAGGCTCCACAAAAGGTGCTCTTGGCGTTTCTATTACCTACACGCCAGTGA 1100

TGATATATGCGCTAAAGGTGAGTGGCGGCGACTGCTAGGGCTTCTGCACCTTTTGGTCTTCTGAAATTGTGCTTTTACCTTCGGGTACATGACATTCGT 1200

CTACTTTTCAGAGTACAAAATAAGSTGCGCTCACTATGAGAGCAGTAGTTTCACTCTCTTTGGGGGTGTACTCAGCCATAGAAAACCTGGAAATTCATCACC 1300

TTCAGATGCGGTTTGTGCTTAGGCGGCAAGTACATTTCTGGCCCCCTGCCACCAAGTTGAAAGTGC CGCAGGCTTTTCATCGATTGCGGCAAAATGATA 1400

ACCAGGCATTTTGTGCTCGGCGTCCCGGCTCCACTACGGTCAACGGCACATTTGGTGC CGGGTTAAAAAGCCTCGTGTGGGTGGCAGAAAAGCTGTTAA 1500

***ORF7 start +1> ***ORF6 stop

ACAGGGAGTGGTAAACCTTGTAAATATGCCAAAATACACCGCAAGCAGCAGAAGAGAAAGAGGGGATGGCCAGCCAGTCAATCAGCTGTGCCAGAT 1600

GTGGGTAAAGATCATCGCTCACCAAAACAGTCCAGAGGCAAGGGACCGGAAAGAAAAATAAGAAGAAAAACCGGAGAAGCCCCATTTCCCTCTAGCG 1700

ACTGAAGATGATGTACAGATCACTTTACCCCTAGTGAGCGTCAATTGTGTCTGTCTGTCATCCAGACCGCTTTAATCAAGCGCTGGGACTTGCACCC 1800

***ORF7 stop

TGTTCAGATTACGGGAGGATAAGTTACACTGTGGAGTTTAGTTTGCCTACGCATCATACTGTGCGCTGATCCGCGTCACAGCATCACCCCTAGCATGATG 1900

GGCTGGCATTCTTGAGGCATCCAGTCTTTGAATTGGAAGATGCGTGGTGAATGGCACTGATTGACATTGTGCTCTAAGTCACCTATTCAATTAGGGC 2000

GACCGTGTGGGGTAAGATTTAATTGGCGAGAACCACACGCGGAAATTAATAAAAAAAAAA 2062

ISU 12/7a/3' terminal (888 – 1413) Lelystad seq (14077 – 14598)	AATGGAGTGG TCCATTAGATG ACTTGTGTGAT TCATAGGACGG GGTCCACAAA AGGTGCTCTTT -ATGG-GAGG --CCTAGACG ATTITTTGCAAT CCATCCATATC GCCCCACAAA AGCTGGTGGT	947 14132
ISU 12/7a/3' terminal (888 – 1413) Lelystad seq (14077 – 14598)	GGCGTTTTC TATTACCTACA GCGCAGTGTAT GATATATGCC CTAAGGTGA GTCCGGGCGCG AGCCTTTAGC ATCACATACA CACCTATTAT GATATACCCC CTTAAGGTGT CACCGCGCGCG	1007 14192
ISU 12/7a/3' terminal (888 – 1413) Lelystad seq (14077 – 14598)	ACTGCTTAGGG CTTCGCAAC TTTTGGTGTCT CCTGAATTGT GCTTTCACTT TCCGGTACAT ACTCCCTGGG CTGTTCGACA TCCCTAATAT TCTGAAGTGT TCGTTTACAT TCGGATACAT	1067 14252
ISU 12/7a/3' terminal (888 – 1413) Lelystad seq (14077 – 14598)	GACATTCGTG CACTTTCAGA GTACAAATAA GGTGGCCCTC ACTATGGGAG CAGTAGTTGC GACATATCTG CATTTTCAAT CCACCAACCG TGTCCGACCTT ACCCTGGGGG CTGTTCGTTGG	1127 14311
ISU 12/7a/3' terminal (888 – 1413) Lelystad seq (14077 – 14598)	ACTCTTTTGG GGGGTGTACT CAGC--CATTA GAAACCTGGA AATTATATCAG CTCCAGATGC -CCCTTCTGT GGGGTGTTTA CAGCTTACACA GAGTCTATGGA AGTTTATCAG TTCCAGATGC	1185 14370
ISU 12/7a/3' terminal (888 – 1413) Lelystad seq (14077 – 14598)	CGTTTGTGCTT TGTACGCCCG CAAGTACATT CTGGCCCCCTG CCCAGCCAGT TGAAGTGC AGATTGTGTTT GCCTTGGCCG GCCATACATT CTGGCCCCCTG CCCATCAGCT AGAAAGTGC	1245 14430
ISU 12/7a/3' terminal (888 – 1413) Lelystad seq (14077 – 14598)	GCAGCTTTTC ATCCGATTTC GCGAAATGAT AACCAAGCAT TTTGTCGTCG GGTCCCGGC GCAGGTCTCC ATTCAATCTC AGGTCTGGT AACCGAGCAT AGCTGTGAG AAAGCCCGCA	1305 14490
ISU 12/7a/3' terminal (888 – 1413) Lelystad seq (14077 – 14598)	TCCACTACGG TCAACGGCAC ATTGGTCCCG GGGTTTAAAA GCCTCGTGT TGGTGGCACA CTAAGATCAG TGAACGGCAC TGTAGTACCA GCACITTCGGA GCCTCGTGT GGGGGGCANA	1365 14550
ISU 12/7a/3' terminal (888 – 1413) Lelystad seq (14077 – 14598)	AAAGCTGTTA AACAGGAGT GGTAAACCTTT GTTAAATATG CCAAAATAA CCAGCTGTTA AAGGAGGAGT GGTAAACCTC GTCAAGTATG GCGCGTAA	1413 14598

FIGURE 9

Lelystad seq (14588 – 14974)	ATGCCCGGTA AAAACCACTA- GCCAGAACAA AAGAAAAGT A- CAG ---C	14632
ISU 12/7a/3' terminal (1403 – 1774)	-----AT GCCAAATAC ACCGCAAGC AGCAGAAGAG	1434
Lelystad seq (14588 – 14974)	TCCGATCGGG AATGGCCAGC CAGTCAATCA ACTGTGCCAG TTGCTGGGTG	14681
ISU 12/7a/3' terminal (1403 – 1774)	AAAGAGCGGG GATGGCCAGC CAGTCAATCA GCTGTGCCAG AITGCTGGG-	1483
Lelystad seq (14588 – 14974)	CAATGATATA GTCCAGCGC CAGCAACCTTA GGGG--A-GG ACAGGCCAAAT	14728
ISU 12/7a/3' terminal (1403 – 1774)	-AA-GATCAT CCGTACCAA AACCACTCCA GAGGCAACGG ACCGG---GA	1528
Lelystad seq (14588 – 14974)	AAGAAAAA-- ---G-----CCGTGAGAAG CCACATTTC CCGTGGGTGC	14766
ISU 12/7a/3' terminal (1403 – 1774)	AAGAAAAATA AGAAGAAAAA CCGGAGAGAG CCCCATTTC CTCACCGAG	1578
Lelystad seq (14588 – 14974)	TGAAGATGAC ATCGGCACC ACCTACCCA GACTGACGC TCCGTGTCT	14816
ISU 12/7a/3' terminal (1403 – 1774)	TGAAGATGAT GTCAACATC AGTTTACCCC TAGTGACCGT CAATTGTGTC	1628
Lelystad seq (14588 – 14974)	TGCAATCGAT CCAGACCGT TTCAATCAAG GCGGAGGAG -TGGTGGCT	14865
ISU 12/7a/3' terminal (1403 – 1774)	TGTGTCAT CCAGACCGC TTTAATCAAG GCGTGGGAG TTGGACG-C	1677
Lelystad seq (14588 – 14974)	TTCAITCCAGC GCGAAGGTCA GTTTACAGT TCAGTTTATG CTGCGCGTTG	14915
ISU 12/7a/3' terminal (1403 – 1774)	GTCAATTC GGCAGATTA GTTACACTG GAGTTTAGT TTCCCTACCC	1727
Lelystad seq (14588 – 14974)	CTCATACAGT GCGCCTGAT TTGGGTGAGTT CTACATCCGC CAGTCAGGT	14965
ISU 12/7a/3' terminal (1403 – 1774)	ATCATACTGT GCGCCTGATC CCGGTACAG CATCACCG-T CAG-CATCA-	1774
Lelystad seq (14588 – 14974)	GCAAGTTAA	14974
ISU 12/7a/3' terminal (1403 – 1774)		1774

FIGURE 10

ISU 12/7a/3' terminal (1775 – 1938)	TGGCGTGGCA TTCTTGAGGC ATCCAGTGT TTGAATTGGA	1814
Lelystad seq (14975 – 15101)	-----TT	14976
ISU 12/7a/3' terminal (1775 – 1938)	ACAATGGCTG GTGAATGGCA CTGATTGACA TTGTCCTCT	1854
Lelystad seq (14975 – 15101)	TGACAGTCAG CTGAATGGCC GCGATTGGCG TGTGCGCTCT	15016
ISU 12/7a/3' terminal (1775 – 1938)	AAGTCACCTA TTCAATTAGG GCGACCTGT GCGGGTAACA	1800
Lelystad seq (14975 – 15101)	GAGTCACCTA TTCAATTAGG GCGATCACAT GCGGGTCATA	15056
ISU 12/7a/3' terminal (1775 – 1938)	TTTAAATT-GG GGAGAACCAC ACGGCCGAAA TTAAAAAAA	1933
Lelystad seq (14975 – 15101)	CTTAAATCAGG GAGGAACCAT GTGACCCAAA TTAAAAAAA	15096
ISU 12/7a/3' terminal (1775 – 1938)	AAAAA	1938
Lelystad seq (14975 – 15101)	AAAAA	15101

FIGURE 11

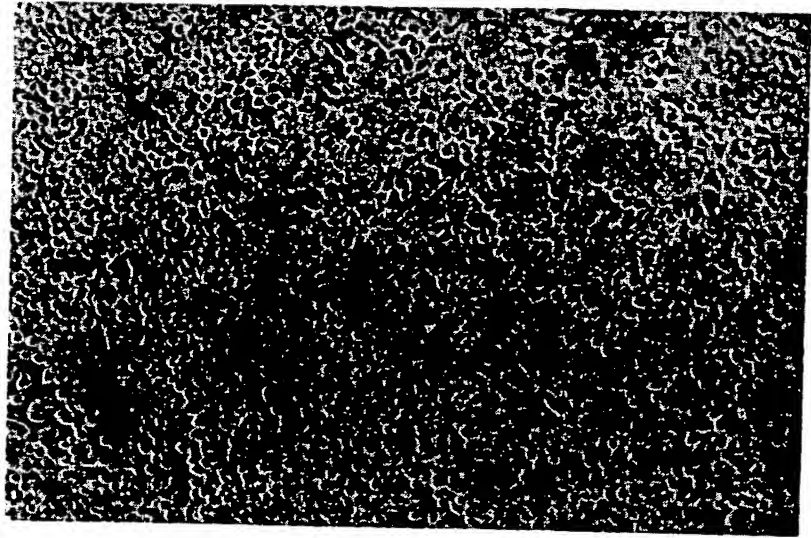


FIGURE 12

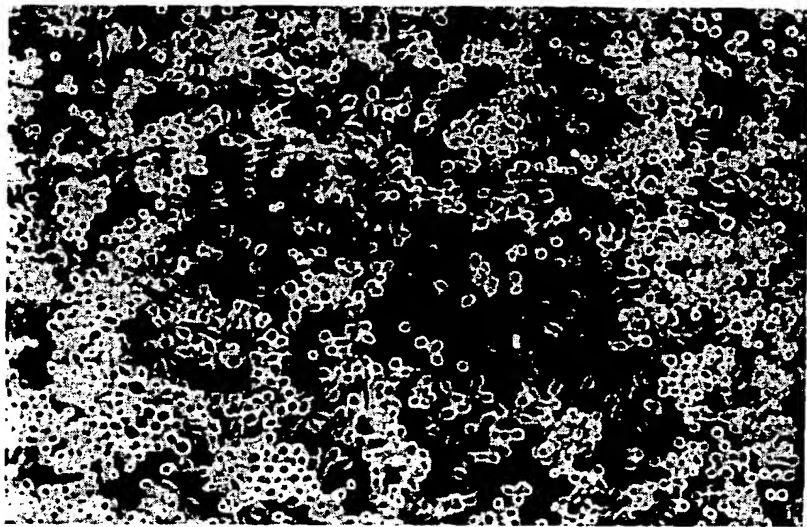


FIGURE 13

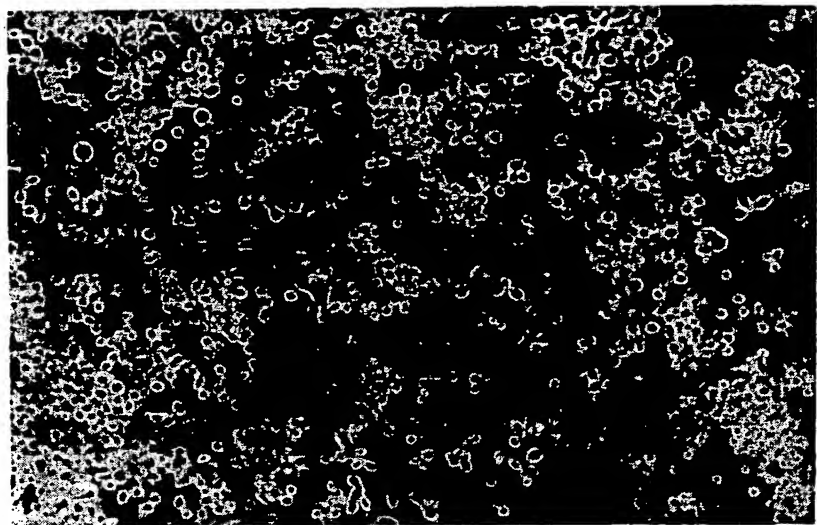


FIGURE 14

SM E M NP E+M+NP SM



FIGURE 15

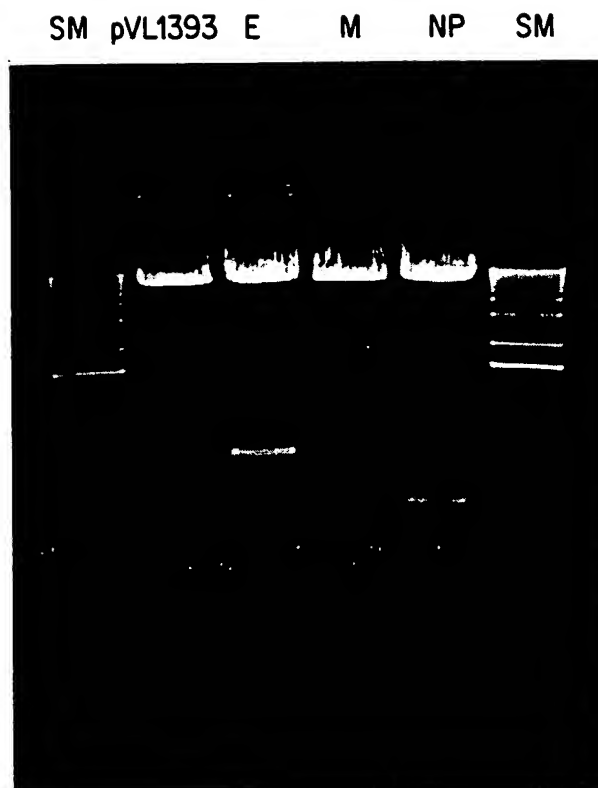


FIGURE 16

FIGURE 17

ORF 6 start		
VR 2385	+ 1> ATGAGTCTGCTCTAGATGACTTCTGTCTGATAGACGGCTCCACAAAGGTGCTCTTGGCGTCTTCTATTACCTACACGCCAGTGATATATGCCC	100
ISU-1894	...G.....C.....T.....T.....	100
ISU-22	...G.....C.....T.....T.....	100
ISU-79	...G.....C.....T.....T.....	100
ISU-55	...G.....C.....T.....T.....	100
ISU-3927	...G.....C.....T.....T.....	100
LV	...G-A-G.C...C...T...T...CA.C...CCT.TC...CG...C.CG.GC.A...C...AGC...C...A...TA.A...C...	97
VR 2385	TAAAGGTGAGTCGGCGCCGACTGCTAGGGCTTCTGCACCTTTTGGTCTTCTGAAATGTGCTTTACCTTCGGGTACATGACATTCGTGCACTTTTCAGAG	200
ISU-1894A.....	200
ISU-22	...G.....A.T.....C.....A.....	200
ISU-79	...A.A.....A.T.....A.....	200
ISU-55	...A.A.....A.T.....T.T.....G.....	200
ISU-3927	...A.A.....A.T.....T.T.....A.....AT...T...ATC	199
LV	...T...TCA...C.G...GT...A.CC.AA.A...T...C...T.C...T.A...A...AT...T...ATC	199
VR 2385	TACAAATAAGGTTCGGCTCACTATGGGAGCAGTAGTTGCACTCCTTTGGGGGGTGTACTCAGC--CATAGAAACCTGGAAATTCATCACTCCAGATGCC	298
ISU-1894G.....	298
ISU-22	...A.....G.....	298
ISU-79	...C.....G.....	298
ISU-55	...C.....G.....	298
ISU-3927	...C.....G.....	298
LV	...C...CCGT...A.T...CC...G...T...T...C...CCT.C...T...TTA...TT...C...GT.A...G...T...T...A	295
VR 2385	GTTTGTGCTTGTCTAGGCGCGAAGTACATTCTGGCCCCCTGCCACCACGTTGAAAGTGCCGCGAGGCTTTCATCCGATTGCGGCAAAATGATAACCCAGCATT	398
ISU-1894	398
ISU-22	398
ISU-79T.....A.....	398
ISU-55T.....G.....	398
ISU-3927T.....G.....	398
LV	...A...T.GC...T...GCCA...T...A...T...TC.C...T.A...CT.A...GTC...G...GA...A	395
VR 2385	TGTCGTTCGGCGTCCCGGCTCCACTACGGTCAACGGCACATTTGGTGCCTGGTTTAAAGCCCTCGTGTGGGTGGCAGAAAGCTGTTAAACAGGGAGTG	498
ISU-1894G.....	498
ISU-22	...T.....G.....	498
ISU-79	...T.....G.....	498
ISU-55	...T.....G.....	498
ISU-3927	...T.....G.....	498
LV	...C.CT...GA.AAAG...ACTA...AT.A...G...TC.A...A...A...AC.TCGG...C...C...A.CG...GA...	495
ORF 7 start		
+ 1> *** ORF 6 stop		
VR 2385	GTAACCTTGTGTTAAATATGCCAAATAACACCGGCA-AGCAGCAGAAAGAGAAAGAA-----GGGGGATGGCCAGCCAGTCAATCAGCTGTG	582
ISU-1894	...C.....A.....	582
ISU-22	...C.....A.T.....	582
ISU-79	...C.....A.....	582
ISU-55	...C.....A.....	582
ISU-3927	...C.....A.....	582
LV	...T...C...C...G...G.CGG...A.A...G...AAGTACAGCTCCGAT...A...A...	591
VR 2385	CCAGATGCTGGGT--AA-GATCATGCTTCACCAAAACAGTCCAGAGGCAAGGACCGGAAAGAAAAATAAGAAGAAAAACCCGAGAAGCCCCATTTC	679
ISU-1894G.....T.....	679
ISU-22	...C.....G.....T.....	679
ISU-79	...C.....G.....T.....	679
ISU-55	...C.....G.....T.....	679
ISU-3927	...A.....C.G.....T.....	679
LV	...T...GC...T...A.AGT.C...G...CCT.G...C...GCC...A...G...T...A...T	679
VR 2385	CCTCTAGCGACTGAAGATGATGTCAGACATCACTTTACCCCTAGTGAGCGTCAATTTGTGTCGTGCTCAATCCAGACCGCCTTTAATCAAGGCGCTGGGA	779
ISU-1894G.....	779
ISU-22	...C.....G.....	779
ISU-79	...C.....A.T.....	779
ISU-55	...C...T...G...G...A...A...	779
ISU-3927	...C...C...G...T...G...	779
LV	...C...G...TG...CA.C.G...C...C...AG.C...A...CTCC.C...CT...CAA...G...G...T...C...A...A...	779
VR 2385	CTTGCAACC-CTGTCAATTCAGGAGGATAAGTTACACTGTGGAGTTTGTGCTGTGCTCAATCCAGACCGCCTTTAATCAAGGCGCTGGGA	877
ISU-1894A.....T.....	877
ISU-22	...C.....T.....	877
ISU-79	...T.....G.....G...	877
ISU-55	...C...T...T...A...G...G...T...G...C...	877
ISU-3927	...C...T...T...A...G...G...T...G...C...	877
LV	...GT.G...T...TCCAGC...A.G.C...TTCAG...T...TGC...GGTTC...A...T...G...TT.TA...T.G	878
*** ORF 7 stop		
VR 2385	TCAG-CA-----TGA	886
ISU-1894	886
ISU-22	886
ISU-79	886
ISU-55	886
ISU-3927	886
LV	...C...T...GGGTGCAAGT.A.	898

A

VR 2385 ORF6	MESSLDDFCHDSTAPQKVLLAFSITYTPVMYALKVSRGRLGLLHLLVFLNCAFTFGYMTFVHFQSTNKVALTMGAVVALLWGVSAIETWKFITSRCR	100
ISU-1894 ORF6	.G.....I.....	100
ISU-22 ORF6	.G.....I.....	100
ISU-55 ORF6	.G.....I.....	100
ISU-79 ORF6	.G.....Y.....I.....M.....	100
ISU-3927 ORF6	.G.....N.....I.....E.....R.....	100
LV ORF6	.G-G...N.PI.A.LV...I.....I.I...S.....Y.....R.....L.....FT.S.....	99
PRRSV-10 ORF6	.G-G...N.PI.A.LV...I.....I.I...S.....Y.....R.....L.....FT.S.....	99
LDV-C ORF2	.G-G.-E..DQTSWY.-IFI...L...IA...S...F..T.A.IVNIFI.I...CVS.V.LMYH.-SV..TI..SL...I..V..I.TLVKIVDWLVI...	96
LDV-P ORF2	.G-G.-E..DQTSWY.-I.I...L...IA...S...F..T.A.IVNIFI.I...CVS.V.LMYH.-SV..TI..SL...I..V..I.TLVKIVNWMVL...	96

VR 2385 ORF6	LCLLGRKYILAPAHVESAAGFHPAANDNH-----AFVVRRPGSTTVNGTLVPLKSLVLGGRKAVKQGVNVLVKY-AK	183
ISU-1894 ORF6	174
ISU-22 ORF6	174
ISU-55 ORF6	174
ISU-79 ORF6	174
ISU-3927 ORF6R.....K.....	174
LV ORF6	.C...R.....L.S.S.SG.R-----YA..K..L.S.....R.....KR..R.....-GR	173
PRRSV-10 ORF6	.C...R.....L.S.S.SG.R-----YA..K..L.S.....R.....KR..R.....-GR	173
LDV-C ORF2	.P...S.....PS..D-----TSDGRQSLTTSITT.....K...L...Q...DFQR.....K...SK.A...L.VS.	171
LDV-P ORF2	.F...S.....PS..D-----TSDGRQSLTTSITT.....K...L...Q...DFQR.....K...SK.A...L.VS.	171

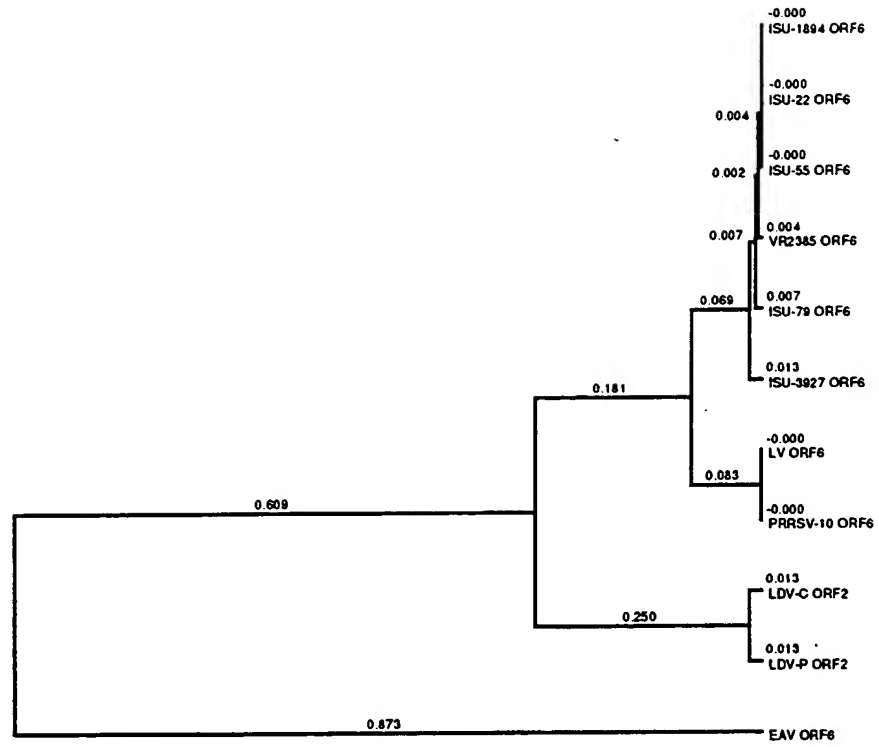
B

VR 2385 ORF7	MPNNTGKQKRRK-----GDGPVNQLCOMLGKIIAHQNSRGKGPCKKKNKKNPEKPHPLATEDDVRHHTPSEKQLCLSSIQTAFNQAGTCTLS	100
ISU-1894 ORF7	...N.....Q.....	93
ISU-22 ORF7	...N.....Q.....	93
ISU-79 ORF7	...N.....Q.....	93
ISU-3927 ORF7	...N...K.....Q.....I..	93
ISU-55 ORF7	...N...K.....Q.....SG.....	93
VR2332 ORF7	...N...TEE.....Q.....	93
LV ORF7	---A..N.SQ..KKSTAPM.N.....L..AM.KS.R---QPR.GOA...K.....A...I...L.QT..S...Q.....AS..	94
PRRSV-10 ORF7	---A..N.SQ..KKSTAPM.N.....L..AM.KS.R---QPR.GOA...K.....A...I...L.QT..S...Q.....PS..	94
LDV-C ORF1	.SQ.KK.GGQN-----AN-----N.LISALLRNAG--N..K.Q.K.-Q-.L...M.GPS.L..VM..N.V.M.R..LV.L...G.Q...V	85
LDV-P ORF1	.SQ.KK.GGQN-----AN-----N.LINALLRNAG--N..K.Q.K.-Q-.L...M.GPS.L..VM..N.V.M.R..LV.L...G.Q...V	85
EAV ORF7	.ASRRSRP.AASF-----RN.R--RRQPTSYNDLLRMFG-----MRVR.PPAQPTQAI.I.EPG.L..DLNQQ..ATLS.NV.RF.MI.H.SL.-A	83

VR 2385 ORF7	DSGRISYTFEFSPLTHHTVRLIRVTASP----SA	134
ISU-1894 ORF7	123
ISU-22 ORF7	123
ISU-79 ORF7	123
ISU-3927 ORF7P.....	123
ISU-55 ORF7	123
VR2332 ORF7	123
LV ORF7	S..KV.FQ...M..VA.....STSASQGAS	128
PRRSV-10 ORF7	S..KV.FQ...M..VA.....STSASQGAS	128
LDV-C ORF1	..G.NF..S.M...A.....NAS.NS-----	115
LDV-P ORF1	..G.NF..S.M...A.....NAS.NS-----	115
EAV ORF7	.A.GLT...SW-V..KQIQ.KVAPP.G-----	110

FIGURE 18

A



B

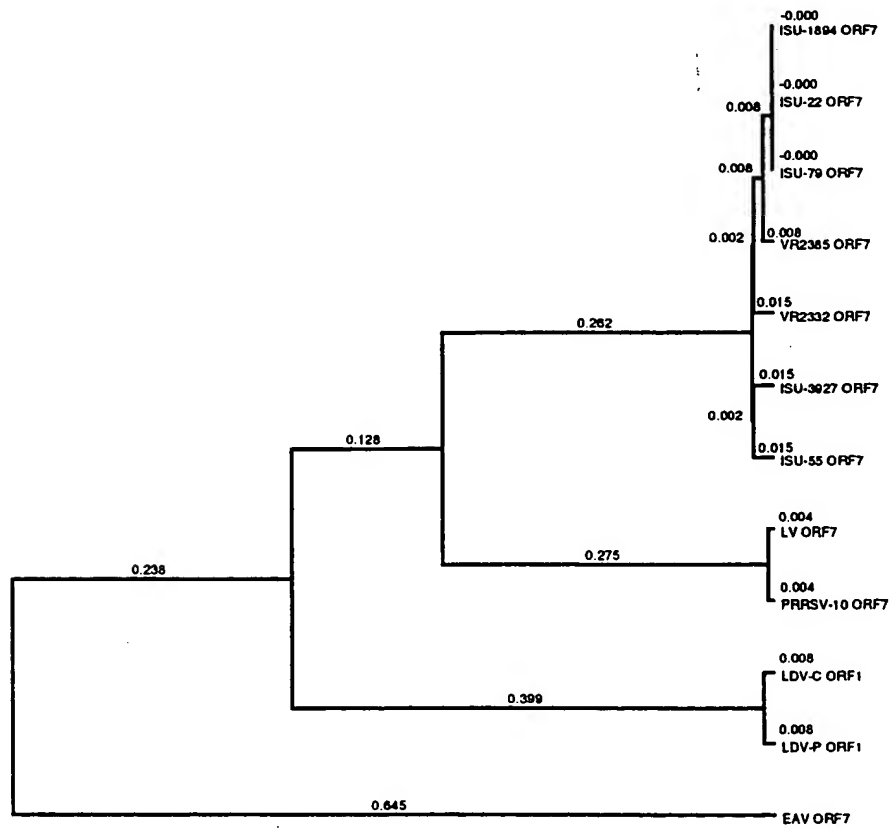


FIGURE 19

+ Start ORF2
 CCTGAATTGAGATGAAATGGGGTCTATGCAAAGCCTTTTGTGACAAAATTGGCCAACCTTTTGTGGATGCTTTCACGGAGTTCTTGGTGTCCATTGTTGAT 100
 ATCATTATATTTTGGCCATTTTGTGTTGGCTTCACCATCGCAGGTGGCTGGTGTCTTTTGTGATCAGATTGGTTTGTCTCCGCGATACTCCGTGCGCGCC 200
 CTGCCATTCACTCTGAGCAATTACAGAAGATCCTATGAGGCCCTTCTCTCTCAGTGCCAGGTGGACATTCCACCTGGGGAACTAAACATCCTTTGGGGA 300
 TGCCTTGGCACCATAGGTGTCAACCCGTGATTGATGAAAATGGTGTGCGGTGGAATGTACCGCATCATGGAAAAAGCAGGACAGGCTGCCTGGAAACAGGT 400
 AGTGAGCGAGGCTACGCTGTCTCGCATTAGTAGTTTGGATGTGGTGGCTCATTTTCAGCATCTTGGCCGCAATTGAAGCCGAGACCTGTAAATATCTGGCC 500
 TCTCGGCTGCCCATGCTACACCACTGCGCATGACAGGCTCAAAATGTAACCATAGTGTATAATAGTACTTTGAATCAGGTGTTTGTCTGTTTTC'CAACCC 600
 + Start ORF3
 CTGGTTCCCGGCCAAAGCTTCATGATTTCCAGCAATGGCTAATAGCTGTACATTCCTCTATATTTTCTCTGTTGCAGCTTCTTGTACTCTTTTGTGTTGT 700
 GCTGTGGTTGCGGGTTCCAAATGCTACGTACTGTTTGTGGTTTCGCTGGTTAGGGGCAATTTTCTTTTGGAACTACGGTGAATTACACGGTGTGCCCGC 800
 *** Stop ORF2 ↓
 CTTGCC'TCACCCGGCAAGCAGCCGAGAGGCC'TACGAACCCGGCAGGTCCCTTTGGTGCAGGATAGGGCATGATCGATGTGGGGAGGACGATCATGATGA 900
 ACTAGGGTTTGTGGTGCCTGTGCGCTCTCCAGCGAAGGCCACTTGACCACTGCTTACGCTGCTTGGCGTCCCTGTCTTTCAGCTATACGGCCCACTTC 1000
 CATCCCGAGATATTCGGGATAGGGAATGTGAGTCGAGTCTATGTTGACATCAAGCACCAATTTCATTTGCGCTGTTTATGATGGGCAGAACACCACTTTC 1100
 + Start ORF4
 CCCACCATGACAACATTTTCAGCGTGTCTTACAGCTATTACCAGCATCAGGTGACGGGGGCAATTGGTTTCACCTAGAAATGGGTGCGTCCCTTCTTTTC 1200
 CTCTTGGTTGGTTTAAATGTCTCTTGGTTTCTCAGGCGTTGCGCTGCAAGCCATGTTTCAGTTGAGTCTTTTCAGACATCAAGACCAACACCAACCGCAG 1300
 CGGCAGGCTTTGCTGTCTTCCAAGACATCAGTTGCCCTTAGGCATCGCAACTCGGCCTCTGAGGCGATTGCAAAAGTCCCTCAGTGCCGCACGGCGATAGG 1400
 *** Stop ORF3
 GACACCCGTGTATATCACTGTCAAGCCAATGTTACCGATGAGAATTATTTGCATTCTCTGATCTTCTCATGCTTTCTTCTTGGCTTTTCTATGCTTCT 1500
 GAGATGAGTGAAAAGGGATTTAAGGTGGTATTTGGCAATGTGTCAAGCATCGTGGCAGTGTGCGTCAACTTCACCAGTTACGTCCAACATGTCAAGGAAT 1600
 TTACCCAACGTTCTTGGTAGTTGACCATGTGCGGCTGCTCCATTTTCATGACGCCCGAGACCATGAGGTGGGCAACTGTTTTCAGCTGTCTTTTACCAT 1700
 ***Stop ORF4 +Start ORF5
 TCTGTTGGCAATTTGAATGTTTAAAGTATGTTGGGGAAAATGCTTTGACCGCGGCTGTTGCTGCAATTTGCTTTTATGAGTGTATCGTGCCTGCTTGT 1799

FIGURE 20

A

Consensus	M.WG.C..K.....L...W.....L..SL...P..CL.SPSQ.G.WSF.S.WFAPR.SVRALPFTL.NYRRSYE..L..C..D.P....KH	100
LV ORF2.	.Q..H.GV.SASCSWTPS.SSLLV.LI-----PF.....Y..G...D.Y...F.E.....F.....P.....GL.PN.RP.V.QFAV..	90
VR2385 ORF2.	.K..L-----AFLTK.AN-FL.MLSRSSWCP.LI..YFW.F..A...V.W...A.D...Y.....S.....AF.SQ.QV.I.TWGT..	93
Consensus	PLGM.WH..VS.LIDEMVSRR.Y..ME..GQAANKQVV.EATL...S.LD.V.HFOHLAA.EA..C..L.SRL.ML..L.....NV...YN.TL..V...	200
LV ORF2.	...F..MR..H.....I.QT..HS.....G....TKL.G..I.T.....V..DS.RF.S...V..KN.AV--G..SLQ..T..DR.ELI	188
VR2385 ORF2.	...L..HK..T.....M.RI..KA.....S....SRI.S..V.A.....I..ET.KY.A...P..HH.RMTGS..TIV..S..NQ.FAV	193
Consensus	FPTPG.RPKL.DF.QWLI.VH.SIFSSVA.S.TLF.VLWLR.P.LR.VFGF.W..A.....	264
LV ORF2.	...T....T..R.....S..A.....S.V...I.....I.A..Y...H.PT---THSS	249
VR2385 ORF2.	...S....H..Q....A..S.....A.C...V....V.M..T....R.LG.IFLNSR-	257

B

Consensus	MA..C.....FLC....Y....A....S..T.CFWPPL..GN.SFELT.NYT.C.PC.T.QAA....EPGR..WC.IGHDRC.E.DHDEL....PSG...	100
LV ORF3.	..HQ.ARFHF...GFIC.LVHS.LASN.SS.L.....AH..T.....I...I.M..S.S...RQRL...NM..K.....E.R.....LMSI...YDN	100
VR2385 ORF3.	..NS.TFLYI...CSFL.SPCC.VVAG.NA.Y.....VR..F.....V..V.P..L.R...AEAY....SL..R.....G.D....GFVV...LSS	100
Consensus	...L...YAWLA.LSPSY.AQFHPE.FGIGNVSRV.VD..HOFICA.HDG.N.T.....NISA....YY.HQ.DGGNWFHLEW.RP.FSSWLVLN.SWFL	200
LV ORF3.	L-K.EGY.....F.....A.....L.....F..KR.....E..H.S.VSTGH....LYAA..H..I.....L..L.....I.....	199
VR2385 ORF3.	ECH.TSA.....S.....T.....I.....Y..IK.....V..Q.T.LPHHD...VLQT..Q..V.....V..F.....V.....	200
Consensus	RRSP.S.VS.R..Q..RPT.P.....S..TS....L.....R.F.....K.S.....	266
LV ORF3.	...V.P..R..IY..IL...R.RLPVSW.FR..IVSD.TGSQQRK.K.PSESRRNVV.P.VLPSTSR	265
VR2385 ORF3.	...A.H..V.VF.TS...P.QRQALL.SK..V--A.GIATRPL.R.A-----LSAARR-	255

C

Consensus	M.A..LF.L.G....VS.APACKPCFS..LSDI.TMTTAAAGF.VLQDI.C.R.....A.E.I...K..QCR.A.GTP.YIT.TANVTDE.YL...DL	100
LV ORF4.	.A.AT..P.A.AQHIM..E.....TH...E.....M.....N.F.PHGUSA.Q.K.SFG.SS...E.V...Q...I.....S..YNA..	100
VR2385 ORF4.	.G.SL..L.V.FKCLL..Q.....SS....K.....A.....S.L.HR--NS.S.A.R--VP...T.I...V...V.....N..HSS..	96
Consensus	LMLS.CLFYASEMSEKGFV.FGNVSG.V..CVNFT.YV.HV...TQ...V....RLLHF.TP..MRWAT..ACLF.IILLAI..	184
LV ORF4.	...A.....I.....V.SA....D..A..TOH..QHHL.IDHI.....L..SA.....TI.....A.....	183
VR2385 ORF4.	...S.....V.....I.AV.....S..Q..KEF..RSLV.DH-V.....M..ET....VL....T.....	179

FIGURE 22

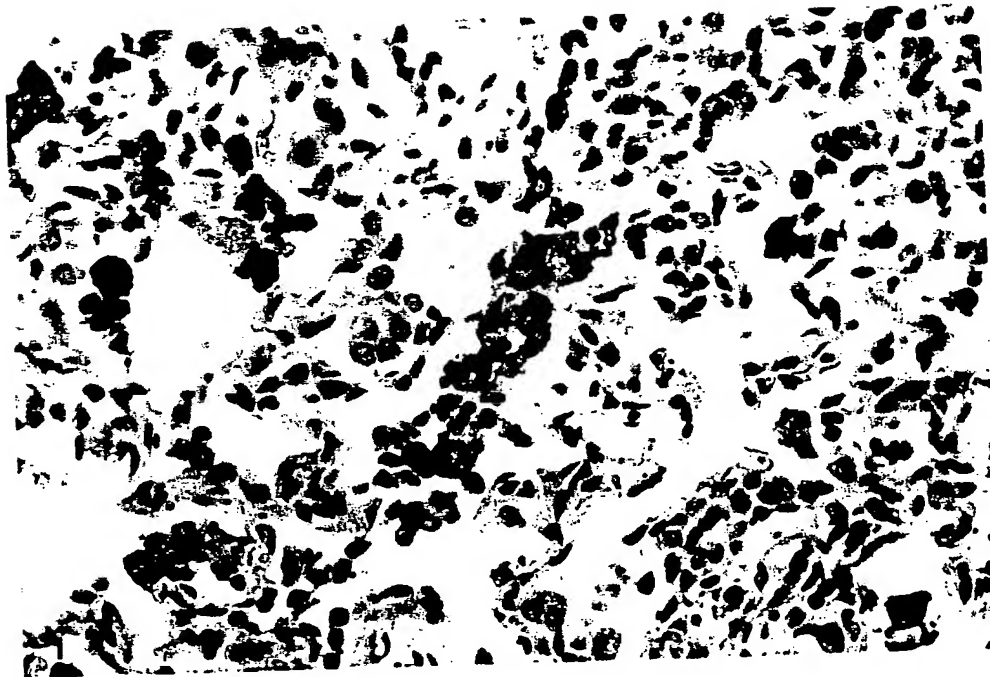


FIGURE 23

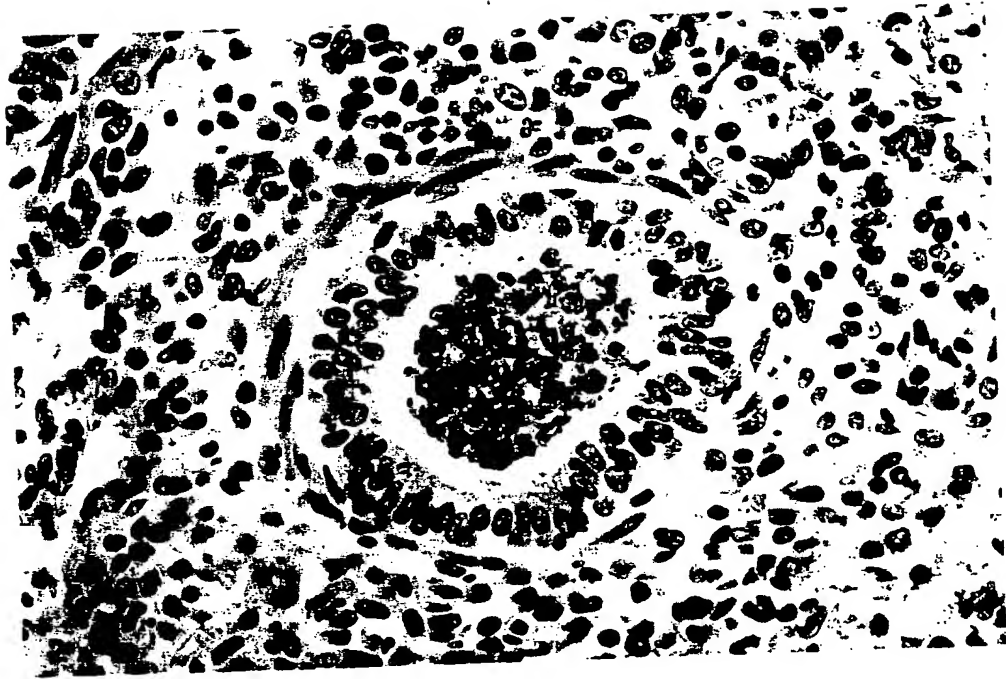


FIGURE 24

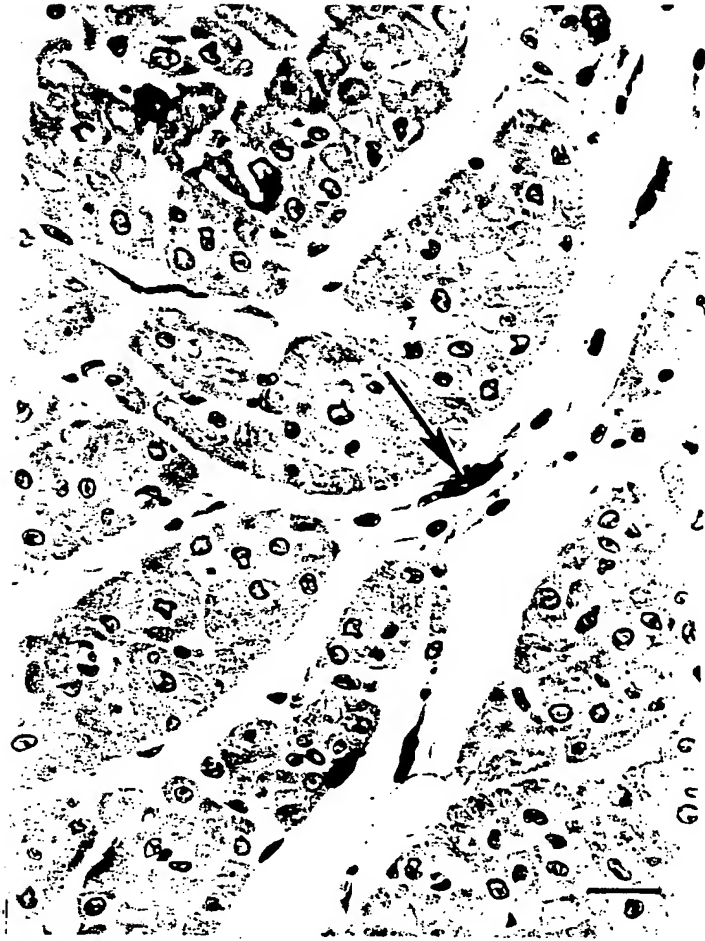


FIGURE 25

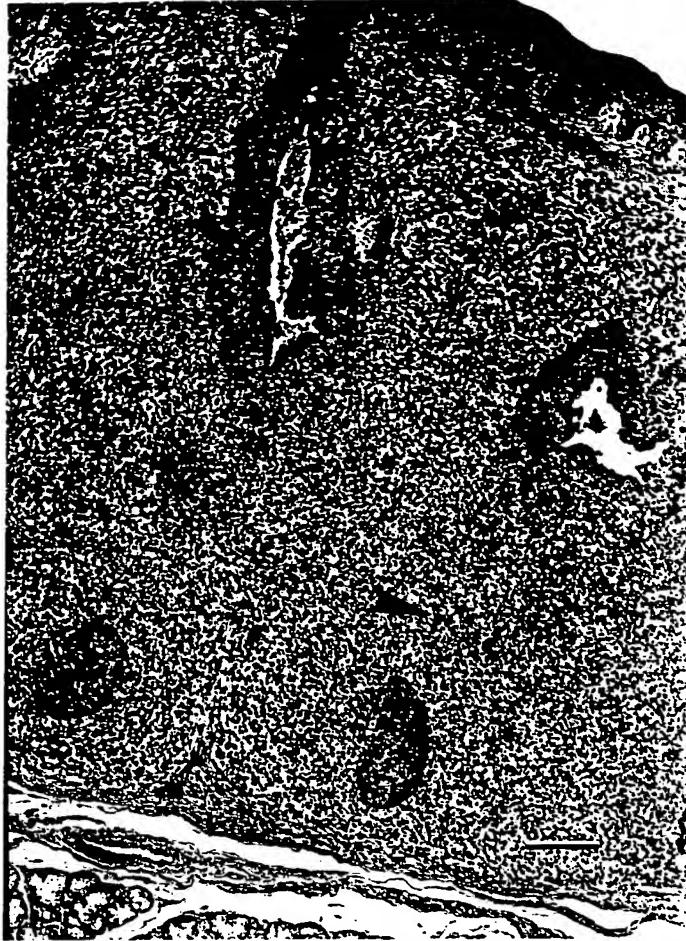


FIGURE 26

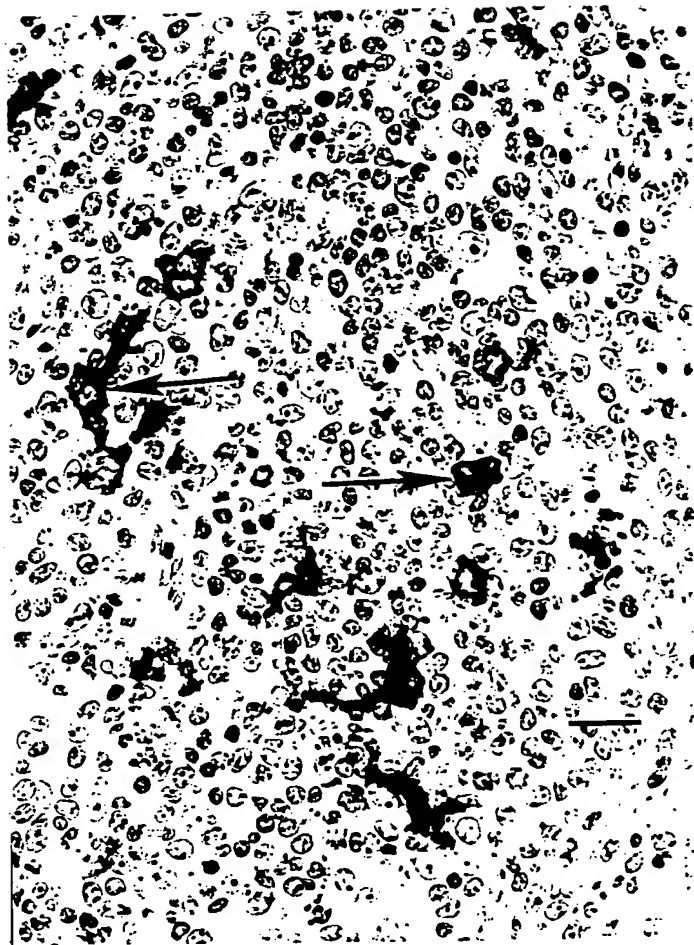


FIGURE 27



FIGURE 28

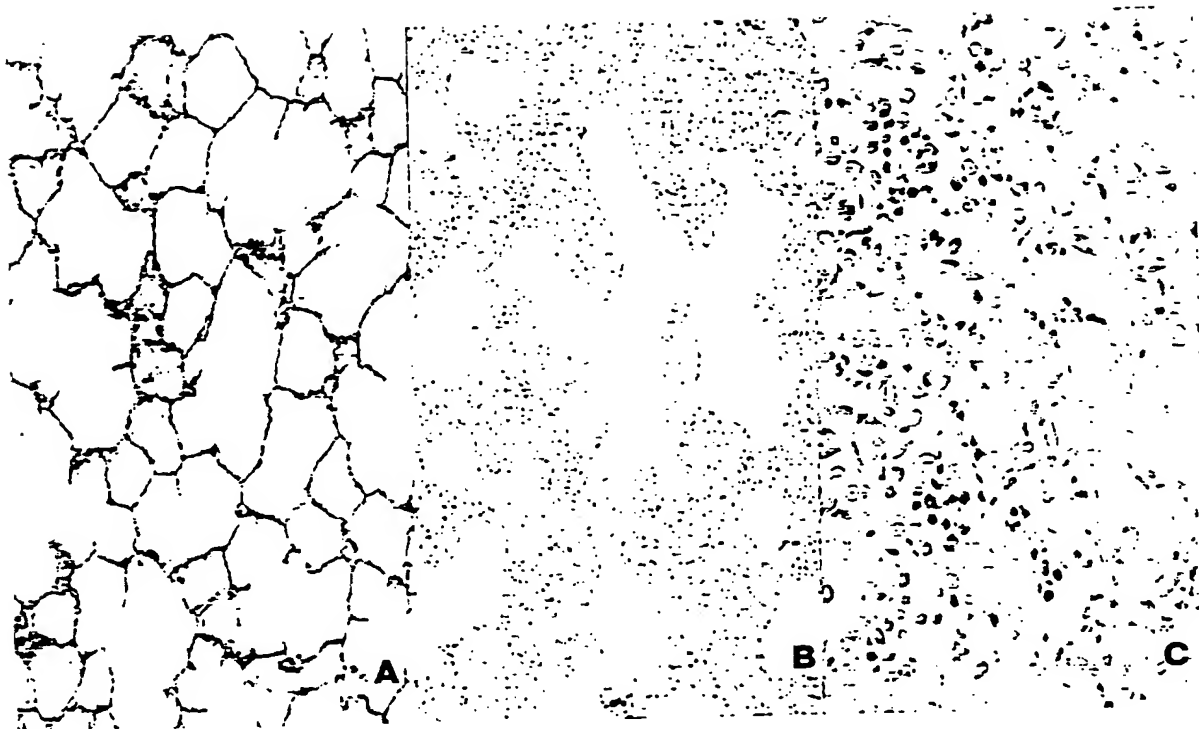
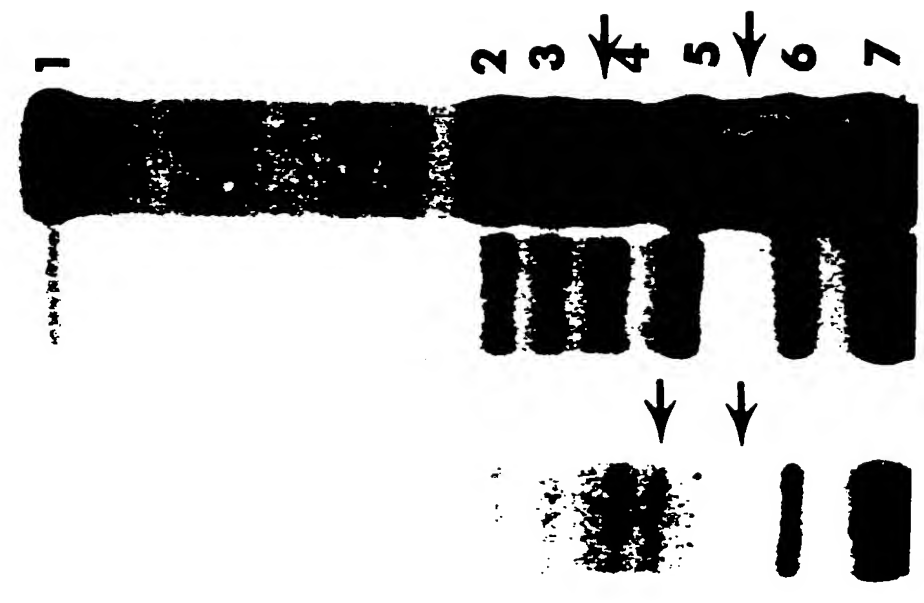


FIGURE 29

1894 3927

22 55 79



A

B

FIGURE 30